



4 October 2011  
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## **APPLICATION A1046 FOOD DERIVED FROM HERBICIDE-TOLERANT SOYBEAN LINE DAS-68416-4 APPROVAL REPORT**

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### **EXECUTIVE SUMMARY**

**Main points are:**

- The Application seeks approval for food derived from a genetically modified (GM), herbicide-tolerant soybean line.
- The Safety Assessment did not identify any potential public health and safety concerns.
- This Report recommends the approval of a draft variation to the Code to include food derived from soybean line DAS-68416-4 in Standard 1.5.2.
- At present, there is no approval to grow this GM soybean line in Australia or New Zealand. Food derived from it would therefore enter the food supply of Australia and New Zealand through imported products.
- In accordance with the labelling laws, food derived from this GM soybean line would have to be labelled as GM if it contains novel DNA or novel protein.

### **Purpose**

Food Standards Australia New Zealand (FSANZ) received an Application from Dow AgroSciences Australia Limited (Dow) on 5 May 2010. The Applicant requested a variation to Standard 1.5.2 – Food produced using Gene Technology, in the *Australia New Zealand Food Standards Code* (the Code), to permit the sale and use of food derived from genetically modified (GM) soybean line DAS-68416-4, conferring herbicide-tolerance.

This Application was assessed under the Major Procedure.

### **Safety Assessment**

The primary objective of FSANZ in developing or varying a food regulatory measure, as stated in s 18 of the *Food Standards Australia New Zealand Act 1991* (FSANZ Act), is the protection of public health and safety. Accordingly, the safety assessment forms the central component in considering an application.

A new GM soybean line, DAS-68416-4, has been developed that is tolerant to the herbicides 2,4-dichlorophenoxyacetic acid (2,4-D) and glufosinate ammonium.

Tolerance to 2,4-D is achieved through the introduction of the *aad-12* gene, from *Delftia acidovorans*, expressing the enzyme aryloxyalkanoate dioxygenase (AAD-12). FSANZ has not assessed this specific protein previously but has assessed a closely related protein, AAD-1, in Application A1042. Tolerance to glufosinate ammonium is conferred by introduction of the *pat* gene from *Streptomyces viridochromogenes* expressing phosphinothricin acetyltransferase (PAT). The PAT protein has been assessed by FSANZ in a number of species including soybean.

FSANZ has completed a comprehensive safety assessment of food derived from soybean line DAS-68416-4 (see **Supporting Document 1**). This assessment included consideration of (i) the genetic modification to the plant; (ii) the potential toxicity and allergenicity of the novel proteins; and (iii) the composition of soybean line DAS-68416-4 compared with that of conventional soybean cultivars. No public health and safety concerns were identified in this assessment.

On the basis of the available evidence, including detailed studies provided by the Applicant, food derived from soybean line DAS-68416-4 is considered as safe and wholesome as food derived from other commercial soybean cultivars.

### **Other assessment considerations**

In assessing the Application, FSANZ has had regard to the following matters as prescribed in s 29 of the FSANZ Act, in addition to considering the safety of food derived from soybean line DAS-68416-4.

- Whether costs that would arise from a food regulatory measure developed or varied as a result of the Application outweigh the direct and indirect benefits to the community, government or industry that would arise from the development or variation of the food regulatory measure.
- Whether there are other measures that would be more cost-effective than a variation to Standard 1.5.2 and could achieve the same end.
- Any relevant New Zealand standards.
- Any other relevant matters.

### **Labelling**

Labelling addresses the objective set out in paragraph 18(1)(b) of the *Food Standards Australia New Zealand Act 1991* (FSANZ Act); that is, the provision of adequate information relating to food to enable consumers to make informed choices. The general labelling requirements will provide consumers with information about the GM status of foods.

In accordance with general labelling provisions, food derived from soybean line DAS-68416-4, if approved, would be required to be labelled as genetically modified if it contains novel DNA or novel protein.

### **Decision**

**To approve the draft variation to Standard 1.5.2 – Food produced using Gene Technology, to include food derived from herbicide-tolerant soybean line DAS-68416-4 in the Schedule.**

## Reasons for Decision

On the basis of the available evidence, the draft variation to the Code to allow the sale and use of food derived from herbicide-tolerant soybean line DAS-68416-4 in Australia and New Zealand has been approved for the following reasons:

- The Safety Assessment did not identify any public health and safety concerns associated with the genetic modification used to produce soybean line DAS-68416-4.
- Food from herbicide-tolerant soybean line DAS-68416-4 is equivalent to that from other commercially available soybean cultivars in terms of its safety for human consumption and nutritional adequacy.
- Labelling of food derived from herbicide-tolerant soybean line DAS-68416-4 will be required in the ingredients list or in conjunction with the name of the food, if it contains novel DNA or novel protein.
- Two regulatory options were considered: (1) rejection of the draft variation to Standard 1.5.2; or (2) approval of the draft variation to permit the sale and use of food derived from soybean line DAS-68416-4.
- Following analysis of the potential costs and benefits of each option on affected parties (consumers, the food industry and government), Option 2, approval of the draft variation, is the preferred option. Under Option 2, the potential benefits to all sectors outweigh the costs associated with the approval.
- There are no relevant New Zealand standards.
- There are no other measures that would be more cost-effective than a variation to Standard 1.5.2 and could achieve the same end.

## Consultation

As this Application was assessed as a Major Procedure, there were two rounds of public comment. Consultation on the 1<sup>st</sup> Assessment was conducted over a period of six weeks; six submissions were received. Consultation on the 2<sup>nd</sup> Assessment was conducted over a period of four weeks; five were received. A summary of these is provided in this Report at **Attachment 2**.

FSANZ has taken all submitters' comments into consideration in completing the assessment of this Application, and has addressed issues, particularly those relevant to the safety of food derived from soybean line DAS-68416-4. Additional information was incorporated into the Safety Assessment where necessary.

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## **SUPPORTING DOCUMENT**

The following material, which was used in the preparation of this Approval Report, is available on the FSANZ website at

<http://www.foodstandards.gov.au/foodstandards/applications/applicationa1046food4807.cfm>

SD1: Safety Assessment Report: Application A1046 – Food Derived from Herbicide-Tolerant Soybean Line DAS-68416-4

## **INTRODUCTION**

On 5 May 2010, Dow AgroSciences Australia Limited (Dow) submitted an Application seeking approval for food derived from soybean line DAS-68416-4 under Standard 1.5.2 – Food produced using Gene Technology, in the *Australia New Zealand Food Standards Code* (the Code).

Soybean line DAS-68416-4 has been genetically modified (GM) to be tolerant to the herbicides 2,4-dichlorophenoxyacetic acid (2,4-D) and glufosinate ammonium. The purpose of the genetic modification is to provide soybean growers with a broader weed management option. Tolerance to 2,4-D has been conferred by the expression of the *aad-12* gene from *Delftia acidovorans* encoding an aryloxyalkanoate dioxygenase enzyme, AAD-12. FSANZ has not previously assessed this specific protein but has assessed a closely related protein, AAD-1, in Application A1042. Tolerance to glufosinate ammonium is conferred by expression of the *pat* gene from *Streptomyces viridochromogenes* encoding phosphinothricin acetyltransferase (PAT). The PAT enzyme has been assessed by FSANZ in a number of crop species including soybean.

FSANZ has completed a scientific evaluation of food derived from soybean line DAS-68416-4 according to FSANZ guidelines (FSANZ 2007) to assess its safety for human consumption. The 1<sup>st</sup> Assessment Report prepared in relation this Application was released in February 2011 for a six-week public consultation period. Issues raised in submissions were considered and considered as part of the development of a draft variation to Standard 1.5.2, which was released in July 2011 for a four week public consultation period. Submissions relating to the 2<sup>nd</sup> Assessment Report have been summarised in **Attachment 2** to this Report.

### **1. The Issue / Problem**

The Applicant has developed GM soybean line DAS-68416-4. Pre-market approval is necessary before food derived from this line may enter the Australian and New Zealand food supply. A variation to the Code, listing food derived from soybean line DAS-68416-4, must be approved by the FSANZ Board, and subsequently be notified to the Australia and New Zealand Food Regulation Ministerial Council (Ministerial Council). A variation to the Code may only be gazetted and registered as a legislative instrument once the Ministerial Council process has been finalised.

Soybean line DAS-68416-4 is intended for cultivation in major soybean-producing countries (currently USA, Canada, Argentina and Brazil). Before its release into commercial markets, the Applicant is seeking regulatory approval for soybean line DAS-68416-4 in a number of trading markets, including Australia and New Zealand. This is necessary because once it is cultivated on a commercial-scale, processed soybean products imported into Australia and New Zealand could contain components derived from soybean line DAS-68416-4. The Application was assessed as a Major Procedure.

### **2. Current Standard**

#### **2.1 Background**

Approval of GM foods under Standard 1.5.2 is contingent upon completion of a comprehensive pre-market Safety Assessment. Foods that have been assessed under the Standard, if approved, are listed in the Schedule of the Standard.

## **2.2 Overseas approvals**

Applications concerning soybean line DAS-68416-4 have been made to the appropriate agencies for food, feed and/or environmental approvals in the United States of America, Canada, South Korea, Taiwan, Argentina and the European Union. It is likely that dossiers will be submitted to the regulatory authorities of trade partners for import clearance including in Brazil, Japan, Mexico, Philippines, Colombia and South Africa.

## **3. Objectives**

In developing or varying a food standard, FSANZ is required by its legislation to meet three primary objectives which are set out in s 18 of the FSANZ Act. These are:

- the protection of public health and safety; and
- the provision of adequate information relating to food to enable consumers to make informed choices; and
- the prevention of misleading or deceptive conduct.

In developing and varying standards, FSANZ must also have regard to:

- the need for standards to be based on risk analysis using the best available scientific evidence;
- the promotion of consistency between domestic and international food standards;
- the desirability of an efficient and internationally competitive food industry;
- the promotion of fair trading in food; and
- any written policy guidelines formulated by the Ministerial Council.

## **RISK ASSESSMENT**

Food derived from soybean line DAS-68416-4 has been assessed according to the safety assessment guidelines prepared by FSANZ(2007). The full Safety Assessment is provided in **Supporting Document 1**. The summary and conclusions from the Safety Assessment are presented below.

In addition to information supplied by the Applicant, other available resource material including published scientific literature and general technical information was used in this assessment.

## **4. Risk Assessment Summary**

### **4.1 Safety Assessment Process**

The Safety Assessment of soybean line DAS-68416-4 included the following key elements: a characterisation of the transferred genes, their origin, function and stability in the soybean genome; the changes at the level of DNA, protein and in the whole food; detailed compositional analyses; evaluation of intended and unintended changes; and the potential for the newly expressed proteins to be either allergenic or toxic in humans.

The assessment of soybean line DAS-68416-4 was restricted to food safety and nutritional issues. Any risks related to the release into the environment of GM plants used in food production, the safety of animal feed, or animals consuming feed derived from GM plants, or the safety of food derived from the non-GM (conventional) plant have not been addressed in this assessment.

## **4.2 Outcomes of the Safety Assessment**

Soybean line DAS-68416-4 contains two novel gene cassettes, one containing the *pat* gene and the other containing the *aad-12* gene. There are no antibiotic resistance marker genes present. Comprehensive molecular analyses indicate that there is a single insertion site containing one complete copy of each of the two cassettes. The introduced genetic elements are stably inherited from one generation to the next.

Expression analyses of the AAD-12 and PAT proteins showed that, in the plant parts tested, the AAD-12 is lowest in the roots and grain (approximately 16 µg/g dry weight) and highest in leaves (approximately 55 µg/g dry weight). PAT protein concentrations are much lower than those for AAD-12 but similarly, the leaves contain the highest levels (approximately 11 µg/g dry weight) and the roots contain the lowest levels (approximately 2 µg/g dry weight). Both proteins conform in size and amino acid sequence to that expected, and do not exhibit any post-translational modification including glycosylation.

In relation to potential toxicity and allergenicity, the Applicant did not supply data for the PAT protein but from previous FSANZ assessments it has been concluded it is inherently non-toxic to mammals and does not exhibit any potential to be allergenic to humans. For the AAD-12 protein, bioinformatic studies confirmed the lack of any significant amino acid sequence similarity to known protein toxins or allergens; a digestibility study demonstrated that the protein would be rapidly degraded in the stomach following ingestion; and a thermolability study showed that the protein is inactivated by heating. An acute oral toxicity study in mice also confirmed the absence of toxicity of AAD-12 in animals. Taken together, the evidence indicates that AAD-12 is unlikely to be toxic or allergenic to humans.

With regard to herbicide metabolites, use of PAT to confer tolerance to glufosinate ammonium has been previously considered in a wide range of food crops, including soybean, and therefore glufosinate ammonium residues were not considered in the Safety Assessment. The major residue generated on soybean line DAS-68416-4 as a result of spraying with 2,4-D is dichlorophenol (DCP). This residue is the same as that found on conventional crops sprayed with 2,4-D and would be present at very minor levels; there are no safety concerns.

Detailed compositional analyses were done to establish the nutritional adequacy of seed-derived products from soybean line DAS-68416-4 under four herbicide-spraying regimes.

The compositional data are consistent with the conclusion that there are no biologically significant differences in the levels of key components in seed from soybean line DAS-68416-4 when compared with the non-GM control or with the range of levels found in commercial soybean cultivars.

## **Conclusion**

No potential public health and safety concerns have been identified in the assessment of soybean line DAS-68416-4. On the basis of the data provided in the present Application, and other available information, food derived from soybean line DAS-68416-4 is considered to be as safe for human consumption as food derived from conventional soybean cultivars.

## **RISK MANAGEMENT**

### **5. Issues**

#### **5.1 Labelling**

In accordance with general labelling provisions, food derived from soybean line DAS-68416-4, if approved, would be required to be labelled as genetically modified if it contains novel DNA or novel protein.

Soybean DAS-68416-4 is intended primarily for use as a broad-acre commodity (field soybean) to produce products derived from cracked soybeans, and is not intended for vegetable or garden purposes where food-grade products may include tofu, soybean sprouts, soy milk, and green soybean (e.g. edamame). This latter type of soybean generally has a different size, flavour and texture to field soybean. The main food product from field soybean is oil in which, because of the production process that results in a highly refined product, protein and DNA are not likely to be present; the oil would therefore not require labelling. Products such as protein concentrate, protein isolate and textured flour are likely to contain protein and DNA and would require labelling.

#### **5.2 Detection Methodology**

Recently, the Implementation Sub-Committee (ISC), a sub-committee of the Food Regulation Standing Committee, agreed to the formation of an Expert Advisory Group (EAG), involving laboratory personnel and representatives of the Australian and New Zealand jurisdictions, that would identify and evaluate appropriate methods of analysis associated with all applications to FSANZ, including GM applications. As part of its remit, the EAG will make recommendations to Australian and New Zealand enforcement agencies on suitable methods of analysis. To date, this EAG has not yet been formed but, as part of an application, the Applicant is required to confirm there is a method of analysis that is fit-for-purpose.

For soybean line DAS-68416-4, there is methodology involving the use of the polymerase chain reaction for DNA detection. The methodology has been submitted to the European Commission Joint Research Centre which publishes a GMO Detection Methods database (<http://gmo-crl.jrc.ec.europa.eu/gmomethods/>). Publication of the method will occur after validation and ring trial.

Additionally, the Applicant has developed immunoassay technology for detection of the AAD-12 protein. A description of this technology has been supplied to FSANZ but is currently Confidential Commercial Information. A patent has been filed but the outcome of the patent application is still pending. The method will be released publicly once either the patent is granted or approval for DAS-68416-4 is given in the USA or Canada.

Because of the technology involved, these detection methods are likely to be restricted to specialist laboratories.

### **6. Impact Analysis**

The impact analysis represents likely impacts based on available information. The impact analysis is designed to assist in the process of identifying the affected parties, any alternative options consistent with the objective of the proposed changes, and the potential impacts of any regulatory or non-regulatory provisions.

The Office of Best Practice Regulation (OBPR), in a letter to FSANZ dated 24 November 2010 (reference 12065), provided an exemption from the need of the OBPR to be informed about GM food applications made to FSANZ.

There were no non-regulatory options for this Application. Two regulatory options identified in relation to the proposed variation to Standard 1.5.2 were:

#### **Option 1 – Reject the draft variation**

Reject the draft variation, thus maintaining the *status quo*.

#### **Option 2 – Approve the draft variation**

Approve the draft variation to permit the sale and use of food derived from soybean line DAS-68416-4.

### **6.1 Affected Parties**

The affected parties may include the following:

- Consumers of soybean-containing food products, particularly those concerned about the use of biotechnology to generate new crop varieties.
- Industry sectors:
  - food importers and distributors of wholesale ingredients
  - processors and manufacturers of soybean-containing food products
  - food retailers
- Government:
  - enforcement agencies
  - national Governments, in terms of trade and World Trade Organization (WTO) obligations.

It is the Applicant's intention that soybean line DAS-68416-4 be commercially cultivated primarily in major soybean-growing countries. FSANZ understands there is currently no intention to apply for approval to cultivate this variety in either Australia or New Zealand. The cultivation of any GM crop in Australia or New Zealand could have an impact on the environment, which would need to be independently assessed by the Office of the Gene Technology Regulator (OGTR) in Australia, and the Environmental Risk Management Authority (ERMA) in New Zealand, before commercial release in either country could be permitted.

### **6.2 Benefit Cost Analysis**

FSANZ has a statutory obligation under s 29 of the FSANZ Act to consider the cost/benefit of both options. This is not intended to be an exhaustive, quantitative dollar analysis of the options and, in fact, most of the impacts that are considered cannot be assigned a dollar value. Rather, the analysis seeks to highlight the qualitative impacts of criteria that are relevant to each option. These criteria are deliberately limited to those involving broad areas such as trade, consumer information and compliance.

### 6.2.1 Option 1 – Reject the draft variation

Consumers: Possible restriction in the availability of imported soybean products to those products that do not contain soybean line DAS-68416-4.

No impact on consumers wishing to avoid GM foods, as food from soybean line DAS-68416-4 is not currently permitted in the food supply.

Potential increase in price of imported soybean foods due to requirement for segregation of soybean line DAS-68416-4.

Government: Potential impact if considered inconsistent with WTO obligations but impact would be in terms of trade policy rather than in government revenue.

Industry: Possible restriction on imports of soybean food products if soybean line DAS-68416-4 were to be commercialised overseas.

Potential longer-term impact - any successful WTO challenge has the potential to impact adversely on the food industry.

### 6.2.2 Option 2 – Approve the draft variation

Consumers: Broader availability of imported soybean products as there would be no restriction on imported foods containing soybean line DAS-68416-4.

Potentially, no increase in the prices of imported foods manufactured using comingled soybean products.

Appropriate labelling would allow consumers wishing to avoid certain GM soybean products to do so.

Government: Benefit that if soybean line DAS-68416-4 was detected in soybean imports, approval would ensure compliance of those products with the Code. This would ensure no potential for trade disruption on regulatory grounds.

Approval of soybean line DAS-68416-4 would ensure no conflict with WTO responsibilities.

In the case of approved GM foods, monitoring is required to ensure compliance with the labelling requirements, and in the case of GM foods that have not been approved, monitoring is required to ensure they are not illegally entering the food supply. The costs of monitoring are thus expected to be comparable, whether a GM food is approved or not.

Industry: Importers of processed foods containing soybean derivatives would benefit as foods derived from soybean line DAS-68416-4 would be compliant with the Code, allowing broader market access and increased choice in raw materials. Retailers may be able to offer a broader range of soybean products or imported foods manufactured using soybean derivatives.

Possible cost to food industry as some food ingredients derived from soybean line DAS-68416-4 would be required to be labelled.

## **6.3 Comparison of Options**

As food from soybean line DAS-68416-4 has been found to be as safe as food from conventional cultivars of soybean, Option 1 was likely to be inconsistent with Australia's and New Zealand's WTO obligations.

Option 1 would also offer little benefit to consumers, as approval of soybean line DAS-68416-4 by other countries could limit the availability of imported soybean products in the Australian and New Zealand markets. In addition, Option 1 would result in the requirement for segregation of any products containing soybean line DAS-68416-4 from those containing approved soybean lines which would be likely to increase the costs of imported soybean-derived foods.

Based on the conclusions of the safety assessments, the potential benefits of Option 2 outweighed the potential costs. A variation to Standard 1.5.2 giving approval to food derived from herbicide-tolerant soybean line DAS-68416-4 was therefore the preferred option.

## **COMMUNICATION AND CONSULTATION STRATEGY**

### **7. Communication**

The communication strategy applied to this Application involves emailing/ mailing alerts to subscribers and interested parties, and placing the reports on the FSANZ website. In addition, FSANZ may issue a media release drawing journalists' attention to this Application.

This Report will be available to the public on the FSANZ website and an alert regarding its release sent to major stakeholders. From 1 May 2011, FSANZ has been placing all new applications on the FSANZ website. Over time applications received before 1 May 2011, particularly those that have attracted a lot of public interest, will be added to the website. Application A1046 is already available on the website at <http://www.foodstandards.gov.au/foodstandards/applications/applicationa1046food4807.cfm>. Submissions are also available on the website.

The Applicant and individuals and organisations who made submissions on this Application were notified at each stage of the assessment. The FSANZ Board's decision to approve the variation to the Code has been notified to the Ministerial Council. If the approval of food derived from soybean line DAS-68416-4 is not subject to review by the Ministerial Council, the Applicant and stakeholders, including the public, will be notified of the gazettal of the relevant changes to the Code in the national press and on the website.

### **8. Consultation**

#### **8.1 Public Consultation**

As this Application was assessed under the Major Procedure, there were two rounds of public consultation. During both rounds of consultation, comments were specifically sought on the scientific aspects of this Application, in particular, information relevant to the safety assessment of food derived from soybean line DAS-68416-4.

Public submissions were invited on the 1<sup>st</sup> Assessment Report between 14 February and 28 March 2011. Six submissions were received on the 1<sup>st</sup> Assessment Report and these were summarised in Attachment 2 to the 2<sup>nd</sup> Assessment Report. Issues raised in submissions were considered and addressed in the 2<sup>nd</sup> Assessment Report, which was released for public comment between 6 July and 3 August 2011.

The five submissions received during this second consultation period have been considered in as part of FSANZ's decision. All submissions relating to the 2<sup>nd</sup> Assessment Report have been summarised in **Attachment 2**. FSANZ has taken the submitters' comments relevant to food safety into account in its decision.

### 8.1.1 General issues

Responses to a number of general issues raised, such as the safety of GM food including long-term health effects, GM food labelling, the relevance of animal feeding studies, data used to inform the Safety Assessment, are available from the FSANZ website (see Table 1). In relation to the Safety Assessment, it should be noted that the data submitted by an Applicant and the conduct of the studies are subject to strict requirements outlined in the *Application Handbook*<sup>1</sup>.

In turn, these requirements are based on widely recognised principles for assessing the safety of whole foods. The principles have been established since the 1990s at the international level by bodies such as the Codex Alimentarius Commission, the World Health Organization and the Organisation for Economic Cooperation and Development (OECD). Similar assessment procedures are followed in Canada, Japan, the European Union and the USA.

The Soil & Health Association of New Zealand expressed concern that FSANZ, in carrying out its assessment of the Application, has placed undue weighting on trade issues rather than on consumer health and safety. As stated in the Executive Summary of this Approval Report, the primary objective of FSANZ in developing or varying a food regulatory measure, (see s 18 of the FSANZ Act), is the protection of public health and safety. Accordingly, the Safety Assessment forms the central component in considering an application. If the Safety Assessment identifies a safety concern it is unlikely that the food would be considered for approval. If, on the other hand, the Safety Assessment does not identify any safety concerns, then a number of other statutory obligations, including Australia's and New Zealand's ability to meet their obligations under the WTO, must be considered in relation to the approval.

**Table 1: Sources of Information, available on the FSANZ website, regarding GM Food**

| Issue                                  | Specific web link  |
|--|--|
| Safety of GM food                      | Safety Assessment of Genetically Modified Foods<br><a href="http://www.foodstandards.gov.au/srcfiles/GM%20Foods_text_pp_final.pdf">http://www.foodstandards.gov.au/srcfiles/GM%20Foods_text_pp_final.pdf</a>   |
|  | Frequently Asked Questions on GM foods<br><a href="http://www.foodstandards.gov.au/foodmatters/gmfoods/frequentlyaskedquest3862.cfm">http://www.foodstandards.gov.au/foodmatters/gmfoods/frequentlyaskedquest3862.cfm</a>  |
| Labelling of GM food                   | Appendix 3: Safety Assessment of Genetically Modified Foods<br><a href="http://www.foodstandards.gov.au/srcfiles/GM%20Foods_text_pp_final.pdf">http://www.foodstandards.gov.au/srcfiles/GM%20Foods_text_pp_final.pdf</a>   |
|  | Frequently Asked Questions on GM foods<br>Part III. Labelling of GM Foods<br><a href="http://www.foodstandards.gov.au/foodmatters/gmfoods/frequentlyaskedquest3862.cfm">http://www.foodstandards.gov.au/foodmatters/gmfoods/frequentlyaskedquest3862.cfm</a>                             |
|  | GM Labelling Review Report<br><a href="http://www.foodstandards.gov.au/newsroom/publications/gmlabellingreviewrep2460.cfm">http://www.foodstandards.gov.au/newsroom/publications/gmlabellingreviewrep2460.cfm</a>  |
| Animal feeding studies                 | Section 7.6: Safety Assessment of Genetically Modified Foods<br><a href="http://www.foodstandards.gov.au/srcfiles/GM%20Foods_text_pp_final.pdf">http://www.foodstandards.gov.au/srcfiles/GM%20Foods_text_pp_final.pdf</a>  |
|  | Role of animal feeding studies in the safety assessment of genetically modified foods<br><a href="http://www.foodstandards.gov.au/consumerinformation/gmfoods/roleofanimalfeedings3717.cfm">http://www.foodstandards.gov.au/consumerinformation/gmfoods/roleofanimalfeedings3717.cfm</a> |
| Data used to inform the Safety Assess. | Food Matters<br>GM Foods<br><a href="http://www.foodstandards.gov.au/foodmatters/gmfoods/">http://www.foodstandards.gov.au/foodmatters/gmfoods/</a>  |

<sup>1</sup> The Application Handbook is available at <http://www.foodstandards.gov.au/foodstandards/changingthecode/applicationshandbook.cfm>.

## 8.1.2 Specific issues

A number of issues specific to the assessment of soybean line DAS-68416-4 were raised in submissions from GE Free New Zealand and the Soil and Health Association of New Zealand and are addressed in the following responses.

### 8.1.2.1 The safety of 2,4-D herbicide and its residues<sup>2</sup>

As for any GM application involving herbicide tolerance, FSANZ needed to consider, in Application A1046, two separate aspects that relate to two separate Standards in the Code.

- In relation to Standard 1.5.2 it is paramount to consider in the Safety Assessment whether novel metabolites are produced following the application of a herbicide and, if so, whether these are present in the final food and whether their presence raises any toxicological concerns. In particular, the assessment considers whether appropriate health-based guidance values (i.e. Acceptable Daily Intake [ADI] or Acute reference Dose [ARfD]) need to be established.
- A separate consideration involves Standard 1.4.2 – Maximum Residue Limits. In the case of food entering Australia via imports (i.e. the crop will not be grown in Australia) it may be necessary for FSANZ to amend the Maximum Residue Limit (MRL)<sup>3</sup>. Standard 1.4.2 does not however apply to New Zealand. Instead, the setting of MRLs for imported foods in that country is considered by the Ministry for Agriculture and Forestry (for inclusion in Maximum Residue Limits of Agricultural Compounds – see <http://www.foodsafety.govt.nz/elibrary/industry/register-list-mrl-agricultural-compounds.htm>).

Any food products (whether derived from GM or non-GM sources) sold in both Australia and New Zealand must not have chemical residues greater than the relevant MRL. The MRL for a herbicide is derived from data collected from field trials conducted under Good Agricultural Practice and is a legally enforceable limit. The results from field trials are used to establish an MRL only if the estimated intake of residue(s) does not exceed the ADI or ARfD, i.e. in undertaking a risk-based assessment to support inclusion of an MRL, the key issue is whether, in the context of the Australian/New Zealand diet, the consumption of chemical residues in the food remains below the health-based guidance values. Where necessary to confirm that the level set is not an undue hazard to human health, a dietary exposure assessment may be undertaken.

For GM applications, the process of considering MRLs is separate from the safety considerations under Standard 1.5.2 and, at the time of preparation of this Approval Report still needs to be undertaken with regard to soybean line DAS-68416-4. Variations to both Standard 1.5.2 and Standard 1.4.2/Maximum Residue Limits of Agricultural Compounds, if appropriate, would need to be gazetted before food derived from soybean line DAS-68416-4 could legally be sold in Australia or New Zealand.

FSANZ does not have responsibility for assessing the environmental impacts or safe use of a herbicide other than in the context of a consideration of any food products that may be derived from a crop sprayed with a herbicide.

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<sup>2</sup> A pesticide residue is any specified substance in food, agricultural commodities or animal feed resulting from the use of a pesticide. The term includes any derivatives of a pesticide, such as conversion products, metabolites, reaction products, and impurities that are considered to be of toxicological significance.

<sup>3</sup> For GM crops grown in Australia, establishment of an MRL is done through collaboration with the Australian Pesticides and Veterinary Medicines Authority (APVMA)

With regard to issues raised about the safety of 2,4-D in a food context, the following points are made:

- 2,4-D is already widely and safely used on food crops (JMPR 1974) and 2,4-D MRLs for a variety of plant-derived food commodities have been adopted by Codex ([http://www.codexalimentarius.net/mrls/pestdes/jsp/pest\\_q-e.jsp](http://www.codexalimentarius.net/mrls/pestdes/jsp/pest_q-e.jsp)).
- The Applicant has supplied data to show that no herbicide metabolites are produced in DAS-68416-4 that are not also produced in conventional crops sprayed with the herbicide.
- The compositional analysis of soybean line DAS-68416-4 compared an unsprayed non-GM control with each of four spray treatments involving DAS-68416-4 (see Section 6 of the Safety Assessment). The results indicated that the composition of line DAS-68416-4 whether sprayed or unsprayed was statistically indistinguishable from that of the non-GM control.
- Notwithstanding the above, the US Environmental Protection Agency (EPA) recently concluded (EPA 2005) that, with regard to dietary risk from 2,4-D sprayed on crops, “acute and chronic dietary exposures for food and drinking water do not exceed the Agency’s level of concern; therefore, no mitigation is warranted at this time for any dietary exposure to 2,4-D”.
- Both GE Free NZ and the Soil and Health Association of New Zealand cited a recent paper (Aris and Leblanc, 2011)<sup>4</sup> that deals with pesticides associated with GM crops. GE Free NZ linked the findings concerning the two herbicides (glyphosate and glufosinate ammonium) mentioned in the paper with 2,4-D.

This paper is lacking in credibility since it fails to establish the source of the chemicals in question (an important point to establish since all the chemicals in question are also associated with non-GM sources). Also, the authors did not report or allege any adverse effects from the presence of the chemicals in the human subjects. FSANZ has prepared a Fact Sheet on the paper, available at <http://www.foodstandards.gov.au/consumerinformation/gmfoods/fsanzresponsetostudy5185.cfm>.

- The USDA Forest Service Report (2006)<sup>5</sup> cited by GE Free NZ is a detailed analysis of the literature on 2,4-D exposure as it applies to vegetation management programmes in forestry. The focus is on workers involved in the application of 2,4-D. While, there is undoubtedly justifiable concern when high levels of 2,4-D are ingested, the relevance of this in the food consumption context is doubtful, given the considerable review that has gone into the setting of MRLs for 2,4-D in food products and the stringency with which levels are monitored in food.

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<sup>4</sup> Aris A, Leblanc S (2011) Maternal and fetal exposure to pesticides associated to genetically modified foods in Eastern Townships of Quebec, Canada. *Reproductive Toxicology* 31: 528 – 533.

<sup>5</sup> USDA Forest Service (2006) 2,4-D human health and ecological risk assessment: Final report. Forest Health Protection, United States Department of Agriculture Forest Service, Arlington. [http://www.fs.fed.us/foresthealth/pesticide/pdfs/093006\\_24d.pdf](http://www.fs.fed.us/foresthealth/pesticide/pdfs/093006_24d.pdf)

- The two publications (de la Rosa et al, 2003 and 2005)<sup>6</sup>, alluded to by the Soil and Health Association of New Zealand, dealing with the adverse synergistic effects of herbicides, are similarly not relevant to the food consumption context.

Notably, the levels of herbicide applied in the tests (e.g. 150 mg/kg body weight) are 3 - 4 orders of magnitude higher than the ADIs for the herbicides i.e. the level of exposure under the test conditions would be far higher than anything realistically possible through consumption of sprayed food. Details published in a report of the UK Committee on Toxicity (COT 2002) confirm the low likelihood of synergistic effects of herbicides (or any other type of pesticide) occurring in the food context.

#### 8.1.2.2 The AAD-12 protein

GE Free New Zealand raised a number of concerns as follows:

- *The AAD-12 protein used in several of the safety studies was produced in a bacterial expression system, not in the plant.*

The AAD-12 protein used in the digestibility and acute toxicity studies was obtained from an *in vitro* GM bacterial (*Pseudomonas*) system since it was not possible to obtain sufficient protein from DAS-68416-4. This is a standard procedure and the bacterial species used to synthesise the protein is not important. What is important is that sufficient testing is done to ensure the bacterially-produced protein is structurally and functionally equivalent to the protein expressed in the plant. The Applicant supplied extensive comparative data to confirm this (see Section.4.4 of the Safety Assessment).

- *The acute toxicity study was not undertaken in a rigorous manner.*

The Applicant supplied an acute oral toxicity study for the AAD-12 protein even though the results from the requisite studies (Codex 2003) did not warrant the generation of additional toxicity data. Since an acute toxicity study was supplied, FSANZ evaluated the results. The study was performed according to OECD Guidelines. There were no deaths or clinical signs and all animals had gained weight by study termination. The gross pathology examination revealed no treatment-related adverse effects.

In relation to the GE Free NZ comment that an acute oral toxicity study does not take into account a vegan diet, it is stressed that the purpose of such a study is not to make any kind of evaluation of dietary exposure. It is purely an objective test of whether an exceptionally high dose, which is far higher than any likely level of consumption irrespective of the type of diet, may give rise to any adverse effects.

- *Since AAD-12 does not exist in the plant kingdom, this makes a scientific nonsense of the allergenicity and toxicity search.*

The bioinformatic searches represent one component of the step-wise assessment strategy that is applied to the assessments of potential toxicity and allergenicity.

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<sup>6</sup> de la Rosa, P. (2003). Changes in immune cell populations and the antibody response to *Streptococcus pneumoniae* after exposure to a mixture of herbicides. PhD Thesis, West Virginia University.

de la Rosa, P.; Barnett, J.B.; Schafer, R. (2005). Characterization of thymic atrophy and the mechanism of thymocyte depletion after *in vivo* exposure to a mixture of herbicides. Journal of Toxicology and Environmental Health A 68: 81 – 98.

This approach takes into account evidence from several types of information and data since no single criterion, especially in relation to potential allergenicity, is sufficiently predictive. The databases used in bioinformatic searches contain hundreds of thousands of sequences derived from all living organisms, not just plants. The main objective in undertaking such searches is to assess the extent to which a newly expressed protein is similar in structure to known allergens or toxins. It makes no difference whether the newly expressed protein has previously existed in nature or not as the purpose of the comparison is merely to determine if the protein shares any sequence or structural elements with existing allergens or protein toxins. However, in this instance, the AAD-12 protein produced by soybean DAS-68416-4 has an amino acid sequence that is 99% homologous with the AAD-12 protein already existing in nature.

If, in the searches, there is no match of the query sequence with sequences from a known toxin or allergen then this forms one part of the evidence to be taken into account in determining the potential toxicity or allergenicity of the protein.

- *Exposure modelling should have been conducted to discover whether event DAS-68416-4 could cause life threatening allergy anaphylaxis.*

The weight of evidence from a number of studies indicated that the novel AAD-12 protein in DAS-68416-4 is unlikely to be toxic or allergenic (see Sections 4.5 and 4.6 of the Safety Assessment). There is therefore no legitimate scientific basis for undertaking further assessment of the potential allergenicity of soybean line DAS-68416-4. Given the results of the studies, it can be confidently concluded that the potential allergenicity of DAS-68416-4 would be equivalent to that of other commercially available soybean lines.

- *There is a lack of NOEL/RDI data on the ingestion of the novel protein*

It is likely that GE Free NZ meant to refer to an ADI (Acceptable Daily Intake) rather than an RDI (Recommended Daily Intake). The relationship between NOEL and ADI is explained on the FSANZ website at <http://www.foodstandards.gov.au/scienceandeducation/publications/20thaustraliantotaldietsurveyjanuary2003/20thaustraliantotaldietsurveyfullreport/partc20thatds/appendix5.cfm>

The only conceivable reason for considering a NOEL or ADI for a GM protein would be if the protein in question were not degraded in the gastrointestinal system. Once a protein from any source is degraded, there would be no potential dietary exposure to the functionally active protein. The end products become part of a pool for which it is impossible to be able to identify the source contributors. It is therefore meaningless to assign any NOEL or ADI values for such proteins.

In Section 4.6.3 of the Safety Assessment, the *in vitro* digestibility of the AAD-12 clearly demonstrates that the protein is rapidly digested in gastric juices within 30 s. The acute oral toxicity study further supports the lack of toxicity of the protein.

## **8.2 World Trade Organization (WTO)**

As members of the World Trade Organization (WTO), Australia and New Zealand are obligated to notify WTO member nations where proposed mandatory regulatory measures are inconsistent with any existing or imminent international standards and the proposed measure may have a significant effect on trade.

Varying the Code to allow food derived from soybean line DAS-68416-4 would have a trade enabling effect as it would permit the food to be imported into Australia and New Zealand and sold, where currently it is prohibited.

Therefore, notification to the WTO under Australia's and New Zealand's obligations under either the WTO Technical Barriers to Trade or Sanitary and Phytosanitary Measures Agreements was not considered necessary.

## **CONCLUSION**

### **9. Conclusion and Decision**

#### **Decision**

**To approve the variation to Standard 1.5.2 – Food produced using Gene Technology, to include food derived from herbicide-tolerant soybean line DAS-68416-4 in the Schedule.**

#### **9.1 Reasons for Decision**

The development of a variation to the Code to give approval to the sale and use of food derived from herbicide-tolerant soybean line DAS-68416-4 in Australia and New Zealand is proposed on the basis of the available evidence, for the following reasons:

- The safety assessment did not identify any public health and safety concerns associated with the genetic modification used to produce soybean line DAS-68416-4.
- Food derived from soybean line DAS-68416-4 is equivalent to that derived from the conventional counterpart and other commercially available soybean cultivars in terms of its safety for human consumption and nutritional adequacy.
- Labelling of food derived from soybean line DAS-68416-4 will be required in the ingredients list or in conjunction with the name of the food, if it contains novel DNA or novel protein.
- Two regulatory options were considered: (1) rejection of the Application; or (2) preparation of a draft variation to permit food derived from soybean line DAS-68416-4 in Standard 1.5.2. Following analysis of the potential costs and benefits of each Option on affected parties (consumers, the food industry and government), Option 2, preparation of a draft variation, is the preferred Option. Under Option 2, the potential benefits to all sectors outweigh the costs associated with the approval.
- There are no relevant New Zealand standards.
- There are no other measures that would be more cost-effective than a variation to Standard 1.5.2 and could achieve the same end.

### **10. Implementation and Review**

The proposed variation to the Code is expected to come into effect on gazettal, subject to any request from the Ministerial Council for a review of FSANZ's decision.

## **REFERENCES**

Codex (2003) Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Plants. CAC/GL 45-2003. Codex Alimentarius.

[http://www.codexalimentarius.net/web/standard\\_list.do?lang=en](http://www.codexalimentarius.net/web/standard_list.do?lang=en)

COT (2002) Risk assessment of mixtures of pesticides and similar substances. Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment, UK Food Standards Agency.

<http://cot.food.gov.uk/pdfs/reportindexed.pdf>.

EPA (2005) Reregistration eligibility decision for 2,4-D. EPA 738-R-05-002. United States Environmental Protection Agency. [http://www.epa.gov/oppsrrd1/REDs/24d\\_red.pdf](http://www.epa.gov/oppsrrd1/REDs/24d_red.pdf).

FSANZ (2007) Safety Assessment of Genetically Modified Foods – Guidance Document. Document prepared by Food Standards Australia New Zealand.

<http://www.foodstandards.gov.au/srcfiles/GM%20FINAL%20Sept%2007L%202.pdf>.

JMPR (1974) 290. 2,4-D. WHO Pesticide Residue Series 4, Joint FAO/WHO Meeting on Pesticide Residues. <http://www.inchem.org/documents/jmpr/jmpmono/v074pr13.htm>.

## **ATTACHMENTS**

1. Draft variation to the *Australia New Zealand Food Standards Code*
2. Summary of submissions

**Draft variation to the *Australia New Zealand Food Standards Code***



**Food Standards (Application A1046 – Food derived from Herbicide-tolerant Soybean Line DAS-68416-4) Variation**

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The Board of Food Standards Australia New Zealand gives notice of the making of this variation under section 92 of the *Food Standards Australia New Zealand Act 1991*. The Standard commences on the date specified in clause 3 of this variation.

Dated XXXX

[Signature to be inserted]

Standards Management Officer  
Delegate of the Board of Food Standards Australia New Zealand

**1 Name**

This instrument is the *Food Standards (Application A1046 – Food derived from Herbicide-tolerant Soybean Line DAS-68416-4) Variation*.

**2 Variation to Standards in the Australia New Zealand Food Standards Code**

The Schedule varies the Standards in the *Australia New Zealand Food Standards Code*.

**3 Commencement**

This variation commences **on the date of gazettal**.

**SCHEDULE**

**[1]** *Standard 1.5.2 is varied by inserting in numerical order in the Schedule –*

|  |     |   |  |
|--|-----|---|--|
|  | 7.x | Food derived from herbicide-tolerant soybean line DAS-68416-4 |  |
|--|-----|---|--|

## Attachment 2

### Summary of issues raised in 2<sup>nd</sup> Assessment public submissions

| Submitter                                      | Comments  |
|--|---|
| Ministry of Agriculture and Forestry (NZ)      | <ul style="list-style-type: none"> <li>Neither supports nor opposes approval.</li> <li>Made comments on the 1<sup>st</sup> Assessment and has no further comments.</li> </ul>   |
| Queensland Health (Whole of QLD Govt response) | <ul style="list-style-type: none"> <li>Neither supports nor opposes approval.</li> <li>Requests an update on progress of applications concerning DAS-68416--4 made to other regulatory agencies around the world<sup>7</sup>.</li> <li>Re-affirms concern made in the 1<sup>st</sup> Assessment consultation about compliance testing and the need for testing methodology to be made available to enforcement agencies.</li> </ul>   |
| Food Technology Association of Australia       | <ul style="list-style-type: none"> <li>Supports approval of the Application</li> </ul>  |
| Soil & Health Association of New Zealand       | <ul style="list-style-type: none"> <li>Opposes approval of the Application on the basis of the following:             <ul style="list-style-type: none"> <li>A recent study published by Aris and Leblanc (2011) has shown that toxins from GM plants are able to pass from food to the bloodstream.</li> <li>Testing of foods derived from DAS-68416-4 has been inadequate. The range of negative metabolic, immune and digestive effects that might occur if the food is eaten has not been addressed. No nutritional studies.</li> <li>Lack of independence of study data.</li> <li>The novel genes in DAS-68416-4 have not been considered by FSANZ before.</li> <li>There may be synergistic effects with the use of the two herbicides, that could lead to unexpected health effects (publications by de la Rosa et al are mentioned but the precise details of the references are not provided).</li> <li>The assessment has been carried out with undue weighting towards trade, not consumer health and safety.</li> </ul> </li> </ul> |

<sup>7</sup> This request was also made at 1<sup>st</sup> Assessment consultation but there had been no change to the status of those applications, and there is still no change at the time of preparation of this Approval Report.

| Submitter           | Comments  |
|---------------------|---|
| GE Free New Zealand | <ul style="list-style-type: none"> <li>• Opposes approval of the Application on the basis of the following claims: <ul style="list-style-type: none"> <li>- The lack of NOEL/RDI data on the ingestion of the novel protein and chemical combination does not give confidence that consumers will be protected.</li> <li>- The novel protein (AAD-12) expressed are not known as to their effects as they have not been tested in the animal or human feeding studies.</li> <li>- The new protein line AAD-12 was isolated from the bacteria itself and not the protein expressed in DAS-68416-4. This inability to conduct studies with the newly expressed novel protein does not show safety in equivalence.</li> <li>- Since AAD-12 does not exist in the plant kingdom, this makes a scientific nonsense of the allergenicity and toxicity search. There can be no similar amino acid sequences identified since they have been created especially for the DAS-68416-4 event.</li> <li>- Exposure modelling should have been conducted in light of the detection of immuno -reactivity to discover whether this event could cause life threatening allergy anaphylaxis.</li> <li>- The acute oral toxicity study is a terrible indictment on the poor rigor and seriousness with which FSANZ experts have met their responsibilities. A cyst in the kidney cortex of the mouse must be taken seriously.</li> <li>- The acute oral toxicity study does not take into account the vegetarian and vegan population who eat soy as their main daily protein.</li> <li>- There have been no studies on the synergistic, antagonistic effects that may occur with the ingestion of a variety of GE foods in the diet.</li> <li>- The lack of labelling of the soybean is an abdication of responsibility.</li> <li>- The reliance on applicant's data has not shown impartiality, openness and accountability.</li> <li>- A number of issues with the use of 2,4-D as a herbicide including: <ul style="list-style-type: none"> <li>o 2,4-D has never been used to directly spray on food plants before. Therefore it has never been assessed.</li> <li>o The acceptance that the levels of 2,4-D are the same as those plants that are not sprayed shows no evidence of good decision making.</li> <li>o 2,4-D has eight different formulations, some more able than others to break down into other toxic metabolites including dioxins. There has been a failure to research the potential range of effects depending on which type of 2,4-D is used.</li> <li>o In the residue chemistry studies there is no consideration of overspray, residue build up in the soil or re-uptake of chemical metabolites that might affect the soy crop ergo human health on ingestion.</li> <li>o A recent study published by Aris and Leblanc (2011) has associated high levels of metabolites and genes to GE foods.</li> <li>o Information cited in a USDA Forest Service Report (2006) documents sub-lethal and synergistic effects of 2,4-D in laboratory animals and humans, including neurological and endocrine effects.</li> <li>o There may be unexpected synergistic effects when 2,4-D and glufosinate are sprayed together.</li> <li>o No levels of 2,4-D and its metabolites have been set.</li> <li>o The Safety Assessment has not evaluated the levels of dichlorophenol residue that would cause acute/non-lethal effects.</li> </ul> </li> </ul> </li> </ul> |